1-1-2016

The Role Of Family History In Predicting Dissection Outcomes

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Thesis

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Abstract

Background: Studies have shown a significant association between family history and aortic aneurysm but this relationship has yet to be explored in depth with dissections. This study examined the role of three family histories (dissection, aortic aneurysm, and sudden death) with the objective to find the best indicator of dissection development.

Methods: A total of N=278 patients seen at Yale between 2013-2015 for aortic aneurysm and dissections were enrolled and their family histories obtained. Six indicators were examined 1) family history of dissection 2) family history of aortic aneurysm 3) family history of sudden death 4) family history of dissection or aortic aneurysm 5) family history of dissection or sudden death and 6) family history of dissection or aortic aneurysm or sudden death.

Results: Patients with a family history of dissection or sudden death were 1.73 (p = 0.038; 95% CI 1.03, 2.90) times as likely to have a dissection compared to those with a negative family history. Patients with a positive family history of aortic aneurysm were 2.31 (p = 0.027; 95% CI 1.10, 4.85) times as likely to have a dissection compared to those with a negative family history (adjusted). Patients with a positive family history of dissection or aortic aneurysm or sudden death were 1.80 (p=0.0487; 95% CI 1.00, 3.23) times as likely to have a dissection compared to those with a negative family history (adjusted).

Conclusion: Three indicators were significant in predicting dissection outcomes 1) family history of dissection or sudden death 2) family history of aortic aneurysm and 3) family history of dissection or aortic aneurysm or sudden death. These findings suggest increased screening for patients with positive corresponding family histories.

Background

The rising prevalence of cardiovascular disease (CVD) continues to be one of the greatest public health concerns today. CVDs account for 31% of all deaths worldwide, around 80% of which are either due to a myocardial infarction (MI) or stroke.[1] Studies suggest, however, that many of these MI attributed deaths are in fact due to other cardiovascular events such as an aortic aneurysm or dissection.[2] A report by the Center for Disease Control and Prevention (CDC) showed that among individuals 15-34 years of age, aortic aneurysm was the 18th leading cause of death in the United States while among individuals 55 years of age and older, it was the 15th leading cause of death.[10] This estimate is predicted to be even higher as studies have shown 2 to 7.3% of sudden cardiac deaths are attributable to aortic rupture and dissections.[11-13]

While an aortic aneurysm refers to an enlargement of the aorta, dissection refers to the event in which the inner and middle layers of the aorta suddenly separate.[3, 4] Aneurysms often precede dissections and therefore it is important to study risk factors that affect both aneurysms and dissections. The current literature shows hypertension, high cholesterol, smoking, connective tissue disease, intracranial aneurysm, abdominal aortic aneurysm, temporal arteritis, autoimmune disorder, renal cysts, certain aortic anatomic variants (e.g. bovine aortic arch, direct origin of left vertebral artery from aortic arch, bicuspid aortic valve), and family history of aneurysm disease with thoracic aortic aneurysm and dissection as risk factors for aneurysmal growth.[2, 5]

As 95% of thoracic aortic aneurysms are estimated to remain asymptomatic before developing into fatal cases of dissection or rupture, it is important that risk factors be carefully studied.[2] But even among symptomatic patients, more than 50% of the emergency department presentations are not diagnosed as thoracic aortic aneurysms prior to death.[2] Rather, these cases of cardiac related sudden death are often signed out as myocardial infarction (MI) due to a presentation of chest pain.[2]

Although previous studies have shown a significant association between family history of aortic aneurysm and aneurysmal development, this relationship has yet to be explored in depth with aortic dissections and thus leaves a gap in literature.[6]

As a result, our study looked at the role of family history in predicting dissection outcomes primarily among patients seen at the Yale Aortic Institute, where patients come specifically to be treated for aortic aneurysms and dissections. Three family histories—dissection, aortic aneurysm, and sudden death—in addition to various combinations of these family histories were all studied with the aim to find the best indicator of dissection development. We hypothesized that a positive family history of aortic aneurysm, dissection, and sudden death are all associated with an increase in the likelihood of dissection development.

Materials & Methods

For our study, aortic aneurysm and dissection patients seen by Dr. John Elefteriades at the Yale Aortic Institute between 2013-2015 were enrolled. In general, as prevalence of dissection is

significantly lower than that of aortic aneurysms, dissection patients seen by other surgeons at Yale during this time were also enrolled to fulfill a robust sample size.

Ultimately, N=278 patients were included in the study, where n= 221 (79.50%) had an aortic aneurysm, n=128 (46.04%) had a dissection, and n=96 (34.53%) had both. Of the N=278, 82.46% were Caucasian, 5.61% Black, 2.46% Asian, 2.46% Hispanic, and 0.70% other. 6.32% of the patients refused to answer questions about their race and ethnicity.

Through a systematic medical record review, we collected data on the following variables: age, sex, race, coronary artery disease, hypertension, dissection, aortic aneurysm, and connective tissue disease. With the exception of age and race, all variables were binary. Connective tissue disease was defined to include Marfan syndrome, Loeys-Dietz syndrome, and Ehlers-Danlos syndrome. Dissection also included aortic rupture.

We also collected data on the family history of aortic aneurysm, dissection, and sudden death. Family history was considered positive if anyone within two generations had exhibited these histories. These were self-reported measures recorded by providers during their consultation with patients. However, because consultation only takes place in non-emergent situations, a significant number of dissection patients who presented to the emergency department were missing this information. Thus, to obtain this data, patients were contacted at their homes using the phone numbers provided on their medical records. A total of 96 patients were contacted with a 79.2% response rate. Appropriate approval from the Institutional Review Board (IRB) and Human Investigation Committee (HIC) was obtained.

Analysis was done using SAS, which looked at various associations between our outcome (dissection) and exposure (family history of dissection, aortic aneurysm, and sudden death). Models included Chi Square and logistic regression (unadjusted and adjusted). Covariates included age, sex, race, coronary artery disease, hypertension, aortic aneurysm, and connective tissue disease.

The three family histories were all looked at individually but also in various combinations (dissection or aortic aneurysm, dissection or sudden death, and dissection or aneurysm or sudden death) with the objective to find the best indicator of dissection development. Each of these family histories was modeled separately controlling for covariates.

Results

Statistical analysis showed that among patients with a positive family history of dissection, 55.56% (n=20) of them had a dissection while 44.44% (n=16) did not. Among patients with a positive family history of aortic aneurysm, 50.00% (n=26) of them had a dissection while 50.00% (n=26) did not. And among patients with a positive family history of sudden death, 54.84% (n=34) of them had a dissection while 45.16% (n=28) did not (Figure 1).

We then looked at a logistic regression model, which showed that patients with a positive family history of aortic aneurysm are 1.71 ($p = 0.090$; 95% CI 0.92, 3.18) times as likely to have a dissection compared to those with a negative family history of aortic aneurysm. Following

adjustment for age, sex, coronary artery disease, hypertension, race, aortic aneurysm, family history of aortic dissection, and family history of sudden death, the odds ratio increased to 2.31 (p = 0.027; 95% CI 1.10, 4.85).

We also combined the family histories in three ways (dissection or aortic aneurysm; dissection or sudden death; dissection or aortic aneurysm or sudden death) to examine whether any of them were significant indicators of dissection development. Analysis showed that patients with a family history of either dissection or sudden death were 1.73 (p = 0.038; 95% CI 1.03, 2.90) times as likely to have a dissection compared to those who have a negative family history. However, adjusted for age, sex, coronary artery disease, hypertension, race, aortic aneurysm, and family history of aortic aneurysm, the odds ratio decreased to 1.16 (p = 0.674; 95% CI 0.58, 2.34).

We also examined the family history of dissection or aortic aneurysm or sudden death as an indicator. Analysis showed an unadjusted odds ratio of 1.56 (p =0.070; 95% CI 0.96, 2.53). Following adjustment for age, female, coronary artery disease, hypertension, race, and aortic aneurysm, it showed that patients with a positive family history of dissection or aortic aneurysm or sudden death are 1.80 (p=0.0487; 95% CI 1.00, 3.23) times as likely to have a dissection compared to those with a negative family history.

Discussion

Our results show patients with a family history of aortic aneurysm are 2.31 times more likely to develop a dissection compared to those without a family history of aortic aneurysm. However, family history of dissection was not significantly related to developing a dissection among patients visiting an Aortic clinic.

Possible reasons for this finding include the fact that many potential cases of dissection among family members were instead categorized into family history of aortic aneurysm or sudden death. This is because patients typically develop an aneurysm prior to having a dissection and thus are able to receive appropriate surgical interventions that reduce the chances of dissecting. As a result, many family members that would have populated the family history of dissection group if left untreated instead fell into the family history of aortic aneurysm group. In addition, when dissections do occur, they are often fatal and result in sudden and undiagnosed death.[2, 4] This would have populated the family history of sudden death group rather than the family history of dissection group.

As 20% of all aortic aneurysms are hereditary and aortic aneurysms increases one's likelihood of dissecting, our findings suggest that patients who have a known family history of aortic aneurysm should undergo more rigorous screening.[6, 9] This is of particular importance to the sub-population of patients who have other risk factors for aneurysmal growth.

Our study had several limitations that we would like to address. First, our primary variables of interest—family history of dissection, aortic aneurysm, and sudden death—were all self-reported. Although they were well screened for by providers and researchers conducting the

study, we acknowledge that self-reported measures are vulnerable to subjectivity and bias. Clinically diagnosing all family members would have been ideal. However, this was not feasible or practical given our timeline and resources.

Secondly, family history of sudden death was defined very broadly to include any case of unexpected death with an unknown cause and thus prone to include several cases of death not attributable to aortic aneurysms or dissections. We included this measure aware of this limitation, however, because of the understanding that many cases of dissection are fatal, sudden, and undiagnosed. Our goal was to capture these cases of death. Our reasoning was also shaped by the fact that although not all sudden deaths are attributable to aortic aneurysms and dissections, this likelihood is significantly higher among families in our study as aortic aneurysms and dissections are hereditary.[6, 9]

Third, the sample was a clinical sample obtained from an Aortic Clinic, and therefore all patients had some heart-related medical issues, and therefore, this limits our generalizability and conclusions to among heart patients. Further, studies are needed to assess family history on CVD outcomes among general populations.

In conclusion, our study suggests that patients with known aortic aneurysms in first or second-degree relatives should be screened more rigorously than those without members in their family. This is particularly important for the sub-population of patients who have other risk factors for dissection development such as Marfan syndrome.[5] In addition, our study also suggests the potential to revise surgical guidelines as expedited surgical interventions may save patients from fatal cases of dissection.

Table 1. Description of the Sample According to Whether Subjects Have a Dissection[a]

	Dissection		
Family History	Yes (N = 80)[b]	No (N = 70)[b]	p[c]
Dissection	20 (55.6)	16 (44.4)	0.263
Aortic Aneurysm	26 (50.0)	26 (50.0)	0.088
Sudden Death	34 (54.8)	28 (45.2)	0.084

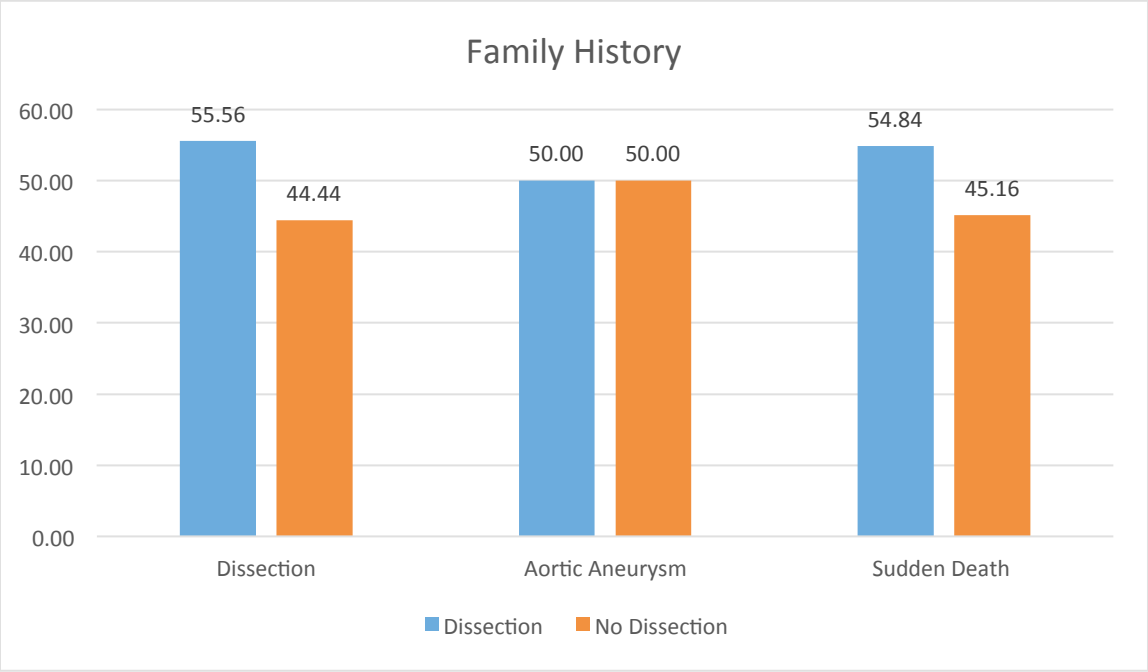
[a] Table values are n (column percentage)
[b] Percentages may not sum to 100% due to rounding
[c] P-value is for χ^2 test

Table 2. Associations between Study Variables and Dissection

Family History	Unadjusted OR (95% CI)	Adjusted OR [b] (95% CI)
Dissection	1.49 (0.74 - 3.02)	1.13 (0.44 - 2.96)
Aortic Aneurysm	1.71 (0.92 - 3.18)	2.31 (1.10 - 4.85)*
Sudden Death	1.65 (0.93 - 2.93)	1.20 (0.57 - 2.51)
AoD or AA[a]	1.30 (0.77 - 2.22)	1.51 (0.77 - 2.95)
AoD or SD[a]	1.73 (1.03 - 2.90)*	1.16 (0.58 - 2.34)
AoD or AA or SD[a]	1.56 (0.96 - 2.53)	1.80 (1.00 - 3.23)*

[a] AoD = dissection, AA = aortic aneurysm, SD = sudden death
[b] Controlled for age, sex, race, coronary artery disease, hypertension, aortic aneurysm, & family history (ones not included in variable)
*Statistically significant

Figure 1. Chi-square associations between dissection and family history



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